REMARKS

Claims 26-67 are pending. The Examiner previously withdrew claims 51-67 from consideration. Claims 26-50 are under consideration.

The Action indicated that Applicants' Response to Final Office Action, filed on November 14, 2006, has been entered. The Action also provided an explanation of how the claims would be rejected for purposes of appeal. Applicants respond to those proposed rejections below.

I. Rejection of Claims 26, 28-35, 39, 40, 43-45, and 47-50 Under 35 U.S.C. § 102(e)

The Examiner maintained the rejection of claims 26, 28-35, 39, 40, 43-45, and 47-50 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,174,670 ("Wittwer"). Action at page 2, item no. 1. Applicants respectfully traverse that rejection.

The Examiner alleged that "Wittwer et al. disclose the method of monitoring hybridization during polymerase chain reaction using of double stranded DNA dye or specific hybridization probes and quantitating amplified DNA. . . ." Action at page 2. The Examiner acknowledged that

> Wittwer et al. do not explicitly disclose combining nucleic acid from the sample with at least one set of reaction composition comprising a first reaction composition and second reaction composition, both specific for the at least one target polynucleotide, wherein the first reaction composition comprises amplification primers specific to at least one target polynucleotide and the second reaction composition comprises a fluorescent indicator and amplification primers specific to at least one target polynucleotide.
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> *Id.* at page 3.

But the Examiner alleged that

> Wittwer et al. disclose that three fluorescence-monitoring techniques for PCR are performed. Each reaction composition has a pair of primers and fluorescence indicator (See column 32, lines 28-61). It is inherent in this teaching that the nucleic acid sample combined at least one set of reaction compositions comprising a first reaction composition and second reaction composition, both specific for the at least one target polynucleotide, wherein the first reaction composition comprises amplification primers specific to at least one target polynucleotide and the second reaction composition comprises a fluorescent indicator and amplification primers specific to at least one target polynucleotide.
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> *Id.*

The Examiner stated that

> [t]he response argues that the Examiner failed to address the claim language 'determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition. . . .' However, Wittwer et al. disclose that three fluorescence-monitoring techniques for PCR are performed. Each reaction composition has a pair of primers and a fluorescence indic[a]tor (See column 32, lines 28-61, fig. 47,). It is inherent in this teaching that the nucleic acid sample combined at least one set of reaction compositions comprising a first reaction composition and second reaction composition.
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> *Id.* at pages 3-4.

The Examiner then alleged that "[s]ince at least both reaction compositions contain target nucleic acid and a fluorescence indic[a]tor, one of the reaction composition[s] would have been used to detect the target nucleic acid in another reaction composition." *Id.* at page 4. The Examiner, however, provided no basis in fact and/or technical reasoning to reasonably support that allegation, as required. As stated in the M.P.E.P.,

> "[t]o establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary

> skill. . . . In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art."
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> M.P.E.P. § 2112 at 2100-47 to 2100-48 (Rev. 5, Aug. 2006).

Notwithstanding the failure to support the statement that "one of the reaction composition[s] would have been used to detect the target nucleic acid in another reaction composition," the Examiner nevertheless concluded that "[b]ased upon the analysis above, the teachings of Wittwer et al. anticipate the limitations of claims." *Id.*

Applicants respectfully traverse the rejection. Applicants continue to assert that Wittwer fails to teach or suggest, either expressly or inherently, "determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition," according to the method of claim 26.

Moreover, to refute the Examiner's unsupported contention that "[s]ince at least both reaction compositions contain target nucleic acid and a fluorescence indic[a]tor, one of the reaction composition[s] would have been used to detect the target nucleic acid in another reaction composition," Applicants offer the following observations.

First, Wittwer provides in Example 9, at col. 32, lines 28-61, that **each** reaction composition comprises a fluorescent indicator and that the fluorescence in **each** reaction composition is determined. Specifically, after describing the reaction compositions for "each of three different fluorescence monitoring methods," Wittwer states that "all amplifications were performed in ten replicates. . . . Fluorescence was acquired for **each** sample. . . . The precision of the three fluorescence monitoring

techniques are compared in Fig. 19D. The mean +/- standard deviations are plotted for **each** point." *Id.* at lines 39-58 (emphasis added).

In addition, Fig. 47 shows flourescence monitoring for **each** reaction composition. Specifically, "Fig. 47 shows a fluorescence ratio v. temperature plot of continuous monitoring during cycle 40 of PCR products of a sample homozygous for the factor V Leiden mutation (solid line), heterozygous for the factor V Leiden mutation (dotted line), and homozygous wild type (alternating dot and dash)." Wittwer at col. 18, lines 50-56. The specification further provides that "[f]our different samples of DNA were tested: human genomic DNA from an individual homozygous for the factor V Leiden mutation; human genomic DNA from a heterozygous individual; human genomic DNA from an individual homozygous for the wild type factor V allele; and a negative control without DNA." *Id.* at col. 44, lines 44-50. Fig. 47 shows the results of fluorescent monitoring of **each** of those different samples.

In summary, Wittwer describes that **each** reaction composition comprises a fluorescent indicator and that the fluorescence in **each** reaction composition is determined. It is clear, then, that Wittwer requires detection of the fluorescent signal in the **same** reaction composition as that containing the target nucleic acid. Thus, contrary to the Examiner's contention, it would **NOT** have been the case that "one of the reaction compositions would have been used to detect the target nucleic acid in another reaction composition." Therefore, Wittwer does not teach or suggest, either expressly or inherently, "determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the

intensity of signal from the fluorescent indicator in the second reaction composition," according to the method of claim 26.

Accordingly, Wittwer does not anticipate independent claim 26 because Wittwer fails to teach or suggest, either expressly or inherently, each and every element of the claim for at least the reasons discussed above. Claims 28-35, 39, 40, 43-45, and 47-50 ultimately depend from claim 26, and thus, also comprise "determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition. . . ." Accordingly, for at least that reason, claims 26, 28-35, 39, 40, 43-45, and 47-50 are not anticipated by Wittwer. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 26, 28-35, 39, 40, 43-45, and 47-50 under 35 U.S.C. § 102(e).

II. Rejection of Claims 27, 36-38, 41, and 42 Under 35 U.S.C. § 103(a)

The Examiner maintained the rejection of claims 27, 36-38, 41, and 42 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wittwer, as applied to claims 26, 28-35, 39, 40, 43-45, and 47-50, and further in view of U.S. Patent No. 6,103,465 ("Johnston-Dow"). Action at page 4, item no. 2. Applicants respectfully traverse that rejection.

The Examiner acknowledged that "Wittwer et al do not disclose a nucleic acid sequencing reaction on the amplification product, the source of DNA sample used as listed in claims 36-38 and determining at least one HLA type." *Id.* The Examiner alleged that "Johnston-Dow et al. disclose a method for typing HLA class I gene and the method involving DNA sequencing techniques. . . ." *Id.* The Examiner further alleged

that "Johnston-Dow et al. also disclose that any source of human nucleic acid can be used [, and that] Johnston-Dow et al. further indicate that HLA typing is performed routinely in connection with many medical indications. . . ." *Id.* at pages 4-5. The Examiner also alleged that "it would have been prima facie obvious to an ordinary skill in the art at the time of the instant invention to apply the sequencing method of Johnston-Dow et al. because the method of Johnston-Dow et al. is applied to the locus-specific nucleic acid amplification followed by sequence-specific detection of the amplified product for the DNA typing of HLA class I gene via DNA sequencing. . . ." *Id.* at page 5.

The Examiner stated that

> [t]he response argues that the same issue as discussed above in connection with claim 26 that 'determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition . . .' was not considered in the previous Office action mailed 8/14/2006. As discussed in section 1, with the same reasons as set forth in section 1, the rejection is maintained.

Id.

Applicants respectfully traverse that rejection. As discussed above in connection with claim 26, because Wittwer describes that fluorescence was detected in **each** reaction composition, it would not have taught or suggested, either expressly or inherently, "determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition," according to the method of claim 26.

Johnston-Dow would have failed to cure the deficiencies of Wittwer. Specifically, Johnston-Dow would have failed to teach or suggest "determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition . . . ," according to the method of claim 26.

Each of claims 27, 36-38, 41, and 42 ultimately depend from claim 26, and thus, also comprise "determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition. . . ." Accordingly, for at least that reason, the combination of Wittwer and Johnston-Dow, asserted by the Examiner, would not have taught or suggested all of the elements of claims 27, 36-38, 41, and 42. Applicants, therefore, respectfully assert that the Examiner has not established a *prima facie* case of obviousness. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 27, 36-38, 41, and 42 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wittwer in view of Johnston-Dow.

Because claims 27, 36-38, 41, and 42 would not have been obvious for at least the reasons discussed above, Applicants do not need to address the Examiner's contentions concerning other elements of those claims. By not addressing those contentions, Applicants in no way acquiesce to those contentions.

III. Rejection of Claim 46 Under 35 U.S.C. § 103(a)

The Examiner maintained the rejection of claim 46 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wittwer, as applied to claims 26, 28-35, 39, 40, 43-

45, and 47-50, and further in view of U.S. Patent No. 6,790,945 ("Lukhtanov"). Action at page 5, item no. 3. Applicants respectfully traverse that rejection.

The Examiner acknowledged that "Wittwer et al. do not disclose using a minor groove binding molecule as a fluorescent indicator." *Id.* at page 6. The Examiner alleged that "Lukhtanov et al. disclose oligonucleotide probes containing a minor groove binding molecule. . . ." *Id.* The Examiner further contended that "[o]ne of ordinary skill in the art at the time of the instant invention would have been motivated to apply the minor groove binding molecule of Lukhta[n]ov et al. because Lukhta[n]ov et al. indicate that the reagents used for labeling oligonucleotide overcome the unfavorable characteristics. . . ." *Id.* The Examiner also alleged that "[i]t would have been prima facie obvious to have minor groove binding molecule as a fluorescent indicator for determining the presence and sequence of at least one target polynucleotide in a sample." *Id.*

The Examiner stated that

> [t]he response argues that the same issue as discussed above in connection with claim 26 that 'determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition . . .' was not considered in the previous Office action mailed 8/14/2006. As discussed in section 1 above, with the same reasons as set forth in section 1, the rejection is maintained.
>
> *Id.*

Applicants respectfully traverse that rejection. As discussed above in connection with claim 26, because Wittwer describes that fluorescence was detected in **each** reaction composition, it would not have taught or suggested, either expressly or inherently, "determining whether the at least one amplification product is present in both

the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition," according to the method of claim 26.

Lukhtanov would have failed to cure the deficiencies of Wittwer. Specifically, Lukhtanov would have failed to teach or suggest "determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition . . . ," according to the method of claim 26.

Claim 46 ultimately depends from claim 26, and thus, also comprises "determining whether the at least one amplification product is present in both the first reaction composition and the second reaction composition from the intensity of signal from the fluorescent indicator in the second reaction composition. . . ." Therefore, for at least that reason, the combination of Wittwer and Lukhtanov, asserted by the Examiner, would not have taught or suggested all of the elements of claim 46. Applicants, therefore, respectfully assert that the Examiner has not established a *prima facie* case of obviousness. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 46 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wittwer in view of Lukhtanov.

Because claim 46 would not have been obvious for at least the reasons discussed above, Applicants do not need to address the Examiner's contentions concerning other elements of that claim. By not addressing those contentions, Applicants in no way acquiesce to those contentions.

CONCLUSION

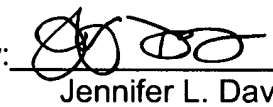
Applicants respectfully request reconsideration of the application and the timely allowance of the pending claims. In the event that the Examiner does not find the claims allowable, Applicants request that the Examiner contact the undersigned at (650) 849-6749 to set up an interview.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: January 16, 2007

By: 

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